Serial No. : 10/055,432
Filed : January 22, 2002

Page : 2 of 15

Amendments to the Claims:

This listing of claims replaces all prior versions and listings of claims in the application:

Listing of Claims:

- 1. (withdrawn) An array comprising:
- a substrate having a plurality of addresses, each address comprising:
- a nucleic acid encoding an amino acid sequence comprising a test amino acid sequence and an affinity tag;
 - a translation effector disposed thereon; and
 - a binding agent that recognizes the affinity tag.
- 2. (withdrawn) The array of claim 1, wherein the binding agent is attached to the substrate.
 - 3. (withdrawn) An array comprising:
 - a substrate with a plurality of addresses, each address comprising:
 - a polypeptide comprising a test amino acid sequence and an affinity tag;
 - a binding agent, that recognizes the affinity tag and is attached to the substrate.
 - 4. (withdrawn) The array of claim 3 wherein a translation extract is disposed thereon.
 - 5. (withdrawn) An array comprising:
 - a substrate with a plurality of addresses, each address comprising:
- a nucleic acid encoding an amino acid sequence comprising a test amino acid sequence and an affinity tag;
 - a binding agent that recognizes the affinity tag.

Serial No. : 10/055,432
Filed : January 22, 2002

Page : 3 of 15

6. (withdrawn) A method comprising:

providing a substrate with a plurality of addresses; and

providing at each address at least (i) a nucleic acid encoding an amino acid sequence comprising a test amino acid sequence and an affinity tag, and (ii) a binding agent that recognizes the affinity tag.

7. (currently amended) A method comprising:

providing a substrate with that comprises a plurality of addresses, each address comprising (i) a nucleic acid encoding a hybrid amino acid sequence comprising a test amino acid sequence and an affinity tag, and (ii) a binding agent that recognizes the affinity tag;

contacting each address of the plurality with a translation effector to thereby translate the hybrid amino acid sequence; and

maintaining the substrate under conditions permissive for the hybrid amino acid sequence to bind the binding agent.

8. (withdrawn) The method of evaluating a protein interaction:

providing a substrate with a plurality of addresses, each address comprising (i) a first nucleic acid encoding a hybrid amino acid sequence comprising a first amino acid sequence and an affinity tag, (ii) a binding agent that recognizes the affinity tag, and (iii) a second nucleic acid encoding a second amino acid sequence;

contacting each address of the plurality with a translation effector to thereby translate the hybrid amino acid sequence;

maintaining the substrate under conditions permissive for the hybrid amino acid sequence to bind binding agent;

detecting the presence of the second amino acid sequence at each of the plurality of addresses.

Attorney's Docket No.: 00246-260001 / 1803

Applicant: LaBaer et al. Serial No.: 10/055,432 : January 22, 2002 . Filed

: 4 of 15 Page

9. (withdrawn) The method of evaluating a protein interaction:

providing a substrate with a plurality of addresses, each address comprising (i) a first nucleic acid encoding a hybrid amino acid sequence comprising a first amino acid sequence and an affinity tag, (ii) a binding agent that recognizes the affinity tag, and (iii) a second nucleic acid encoding a second amino acid sequence;

contacting each address of the plurality with a translation effector to thereby translate the first nucleic acid and the second nucleic acid;

maintaining the substrate under conditions permissive for the hybrid amino acid sequence to bind binding agent;

at each of the plurality of addresses, detecting at least one parameter that is dependent on interaction between a compound that includes the first amino acid sequence and a compound that includes the second amino acid sequence.

10. (withdrawn) A method comprising:

providing (i) a first plurality of nucleic acids, each encoding an amino acid sequence comprising a test amino acid sequence and an affinity tag; (ii) a second plurality of nucleic acids, each encoding an amino acid sequence comprising a test amino acid sequence and a recognition tag; and (iii) a substrate with a plurality of addresses and a binding agent that binds the affinity tag and is attached to the substrate; and

disposing on the substrate, at each address, a nucleic acid of the first plurality and a nucleic acid of the second plurality.

11. (currently amended) A method comprising:

providing a substrate comprising a plurality of addresses, each address of the plurality having a binding agent;

Serial No. : 10/055,432
Filed : January 22, 2002 .

Page : 5 of 15

providing a plurality of nucleic acid sequences, each nucleic acid sequence comprising a sequence encoding a test amino acid sequence and an affinity tag that is recognized by the binding agent;

transmitting, from a server, one or more choices for amino acids to include on the substrate across a network to a user;

receiving at least one selection from the user; and

disposing the one or more nucleic acid sequence corresponding to the selection on an address of the plurality.

- 12. (withdrawn) The method of claim [[6]] 7 further comprising contacting each address of the plurality with a transcription effector.
- 13. (withdrawn) The method of claim 6 further comprising contacting each address of the plurality with a translation effector.
- 14. (withdrawn) The method of claim 6 further comprising contacting each address of the plurality with a transcription effector and a translation effector.
- 15. (withdrawn) The method of claim [[13]] 7 wherein the translation effector comprises a translation extract prepared from cells.
- 16. (withdrawn) The method of claim [[13]] 7 further comprising contacting each address of the plurality with a chaperone.
- 17. (withdrawn) The method of claim 6 further comprising enclosing the substrate in an air- or water- resistant package.

Serial No.: 10/055,432 Filed: January 22, 2002

Page : 6 of 15

18. (withdrawn) The method of claim [[6]] 7 wherein each test amino acid sequence is unique.

- 19. (withdrawn) The method of claim [[6]] 7 wherein the affinity tag is separated from the test amino acid sequence by at least five amino acids.
- 20. (withdrawn) The method of claim [[6]] 7 wherein the affinity tag encoded by the nucleic acid at each address of the plurality is the same.
- 21. (withdrawn) The method of claim [[6]] 7 wherein the affinity tag encoded by the nucleic acid at an address of the plurality differs from at least one other affinity tag in the plurality of addresses.
 - 22. (withdrawn) The method of claim [[6]] 7 wherein the nucleic acid is DNA.
- 23. (withdrawn) The method of claim 22 wherein the nucleic acid is double stranded DNA.
- 24. (withdrawn) The method of claim 22 wherein the nucleic acid comprises an operably linked transcription promoter.
- 25. (withdrawn) The method of claim [[6]] 7 wherein the nucleic acid comprises an internal ribosome entry site.
- 26. (withdrawn) The method of claim [[6]] 7 wherein the nucleic acid comprises a plurality of cistrons.

Serial No.: 10/055,432
Filed: January 22, 2002.

Page : 7 of 15

27. (withdrawn) The method of claim [[6]] 7 wherein the nucleic acid comprises a sequence that encodes a reporter protein.

- 28. (withdrawn) The method of claim 27 wherein the reporter protein can produce or modulate light.
- 29. (withdrawn) The method of claim 6 wherein the transcription promoter is a prokaryotic promoter.
- 30. (withdrawn) The method of claim [[6]] 7 wherein the amino acid sequence comprises an intein.
 - 31. (withdrawn) The method of claim [[6]] 7 wherein the substrate is partitioned.
- 32. (withdrawn) The method of claim [[6]] 7 wherein the substrate comprises at least 1 address per cm².
- 33. (withdrawn) The method of claim 32 wherein the substrate comprises at least 10 addresses per cm².
- 34. (withdrawn) The method of claim [[6]] 7 wherein each address contains less than 1 ng of the nucleic acid.
- 35. (withdrawn) The method of claim [[6]] 7 wherein each address contains less than 10 pg of the nucleic acid.
- 36. (withdrawn) The method of claim [[6]] 7 wherein the binding agent comprises a biological polymer.

Serial No.: 10/055,432
Filed: January 22, 2002

Page : 8 of 15

37. (withdrawn) The method of claim 6 wherein the binding agent is covalently attached to the substrate.

- 38. (withdrawn) The method of claim 6 wherein the binding agent is attached by a bridging moiety.
 - 39. (withdrawn) The method of claim 6 wherein the binding agent is an antibody.
- 40. (withdrawn) The method of claim [[6]] 7 wherein the affinity tag comprises a polypeptide sequence which can chelate metal.
- 41. (withdrawn) The method of claim 40 wherein the affinity tag comprises hexahistidine.
- 42. (withdrawn) The method of claim 6 wherein <u>the</u> affinity tag comprises a protein selected from the group consisting of glutathione-S-transferase, chitin binding protein, cellulase, maltose binding protein, dihydrofolate reductase, and FK506 binding protein (FKBP).
- 43. (withdrawn) The method of claim [[13]] 7 further comprising contacting each address of the plurality with a protein-modifying enzyme.
- 44. (withdrawn) The method of claim [[6]] 7 wherein the nucleic acid comprises a site-specific recombination site.
- 45. (withdrawn) The method of claim [[6]] 7 wherein each address comprises a plurality of nucleic acid sequences, each encoding a unique test amino acid sequence and an affinity tag.

Serial No.: 10/055,432 Filed: January 22, 2002

Page : 9 of 15

46. (withdrawn) The method of claim 6 wherein the providing comprises mechanically delivering the nucleic acid to each address of the plurality of addresses.

- 47. (withdrawn) The method of claim 6 wherein the providing comprises amplifying a template nucleic acid to provide a nucleic acid for each address of the plurality of addresses.
- 48. (previously presented) The method of claim 7 further comprising contacting cells to the substrate and evaluating the cells or a parameter of the cells.
- 49. (previously presented) The method of claim 7 further comprising contacting members of a display library to the substrate.
- 50. (previously presented) The method of claim 7 further comprising contacting a patient sample to the substrate.
- 51. (previously presented) The method of claim 50 further comprising further comprising detecting binding of the patient sample to the array.
- 52. (previously presented) The method of claim 51 further comprising recording results of the detecting in a database.
- 53. (previously presented) The method of claim 7 wherein the test amino acid sequences at the plurality of addresses comprise allergens and/or auto-immune antigens.
- 54. (previously presented) The method of claim 7 wherein the test amino acid sequences at the plurality of addresses comprise naturally occurring sequences.

Serial No.: 10/055,432 Filed: January 22, 2002

Page : 10 of 15

55. (previously presented) The method of claim 54 wherein the test amino acid sequences at the plurality of addresses comprise bacterial antigens.

56. (previously presented) The method of claim 54 wherein the test amino acid sequences at the plurality of addresses comprise viral antigens.

- 57. (previously presented) The method of claim 56 wherein the viral antigens comprise antigens from a rotavirus, hepatitis virus, herpes virus, papilloma virus and/or a retrovirus.
- 58. (previously presented) The method of claim 7 wherein the test amino acid sequences at the plurality of addresses comprise artificial amino acid sequences.
- 59. (previously presented) The method of claim 7 wherein the test amino acid sequences at the plurality of addresses comprise transmembrane proteins whose transmembrane domains have been excised.
- 60. (previously presented) The method of claim 7 wherein the test amino acid sequences at the plurality of addresses comprise randomized amino acid sequences.
- 61. (previously presented) The method of claim 7 wherein the test amino acid sequence comprises an immunoglobulin variable domain.
- 62. (previously presented) The method of claim 7 further comprising contacting endoplasmic reticulum vesicles to the array.
- 63. (previously presented) The method of claim 7 wherein the substrate comprises at least 10 addresses per cm².

Serial No.: 10/055,432
Filed: January 22, 2002

Page : 11 of 15

64. (previously presented) The method of claim 7 wherein each address contains less than 1 ng of the nucleic acid.

- 65. (previously presented) The method of claim 7 wherein each address contains less than 10 pg of the nucleic acid.
- 66. (withdrawn) The method of claim 22 wherein the DNA <u>nucleic acid</u> comprises plasmid DNA.
- 67. (withdrawn) The method of claim 22 wherein the DNA <u>nucleic acid</u> comprises a PCR product.
- 68. (withdrawn) The method of claim [[6]] 7 wherein the providing of nucleic acid at each address comprise the substrate comprises:

providing a collection of nucleic acids, each member of the collection being compatible with a recombinational cloning system and including an open reading frame of interest;

recombining members of the collection with a recipient nucleic acid that comprises a nucleic acid sequence encoding an affinity tag such that the open reading frame is linked in frame to the nucleic acid sequence encoding the affinity tag; and

disposing nucleic acid derived from the recombination at addresses of the plurality of addresses.

- 69. (withdrawn) The method of claim 68 wherein the collection comprises at least 500 members.
- 70. (withdrawn) The method of claim 68 wherein members of the collection are identified by a locator accessible to a robotic system.

Serial No.: 10/055,432
Filed: January 22, 2002.

Page : 12 of 15

71. (withdrawn) The method of claim 68 wherein members of the collection are referenced by a relational database that includes information about storage location and a link to another biological database.

- 72. (previously presented) The method of claim 7 wherein each address further comprises a nucleic acid encoding a modifying enzyme.
- 73. (previously presented) The method of claim 72 wherein the modifying enzyme is varied among the addresses of the plurality.
 - 74. (withdrawn) The method of claim 10 further comprising:

contacting each address of the plurality with a translation effector to thereby translate the nucleic acid of the first plurality and the nucleic acid of the second plurality; and

maintaining the substrate under conditions permissive for the affinity tag to bind the binding agent.

- 75. (withdrawn) The method of claim 74 further comprising washing the substrate to remove the translation extract and unbound polypeptides.
- 76. (withdrawn) The method of claim 75 further comprising detecting the recognition tag at addresses of the plurality of addresses.
- 77. (withdrawn) The method of claim 10 wherein the recognition tag comprises an epitope tag, an enzyme, or a fluorescent protein.
- 78. (withdrawn) The method of claim 11 further comprising providing the substrate to the user.

Serial No.: 10/055,432 Filed: January 22, 2002.

Page : 13 of 15

79. (withdrawn) The method of claim 11 wherein the server is interfaced with a robotic system, and the at least one selection is communicated from the server to the robotic system.

80. (withdrawn) The method of claim 11 wherein the choices are arranged hierarchically.

81. (withdrawn) The method of claim 11 wherein the choices comprise a list of general

user needs.

82. (withdrawn) The method of claim 11 wherein the choices comprise a list of classes

of amino acid sequences.

83. (withdrawn) The method of claim 11 wherein the choices comprise individual amino

acid sequences.

84. (withdrawn) The method of claim 82 wherein the classes comprise entries correlated

with a condition or disease.

85. (withdrawn) The method of claim 82 wherein the classes comprise entries correlated

with a protein family.

86. (withdrawn) The method of claim 82 wherein the classes comprise entries correlated

with an organismal species.

87. (withdrawn) The method of claim 11 wherein the server recommends a control

amino acid sequence based on user selections.

Attorney's Docket No.: 00246-260001 / 1803 Applicant: LaBaer et al.

Serial No.: 10/055,432 Filed : January 22, 2002 . Page : 14 of 15

88. (previously presented) The method of claim 7 further comprising evaluating the substrate for a fluorescence.

- 89. (previously presented) The method of claim 7 further comprising evaluating the substrate using mass spectroscopy.
- 90. (previously presented) The method of claim 7 further comprising evaluating the substrate for a fluorescent property.
- 91. (previously presented) The method of claim 7 further comprising evaluating the substrate for an enzymatic property.
- 92. (previously presented) The method of claim 7 further comprising evaluating the plurality of addresses on the substrate, and recording results of the evaluating in records of a database.
- 93. (previously presented) The method of claim 92 further comprising clustering the records to identify addresses which are related.
- 94. (previously presented) The method of claim 92 further comprising making results of the evaluating accessible to a network of health care providers.
- 95. (previously presented) The method of claim 92 further comprising making results of the evaluating accessible to a physician.